IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Steven A. Bogen and Herbert H. Loeffler		
Application No.:	10/823,368	Group:	1797
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Confirmation No.:	4846		
For:	SLIDE STAINER WITH HEATING		

APPEAL BRIEF

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Sir:

This Appeal Brief is submitted pursuant to the Notice of Appeal received in the U.S. Patent and Trademark Office on June 16, 2008, and in support of the appeal from the final rejection set forth in the Office Action mailed on January 17, 2008. The fee for filing a brief in support of an appeal is enclosed. A Petition for Extension of Time and the appropriate fee are being filed concurrently.

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I. REAL PARTY IN INTEREST

The real party in interest is Dako Denmark A/S. Dako Denmark A/S is the Assignee of the entire right, title and interest in the subject application by virtue of an Assignment recorded on April 7, 2008 at Reel 020762, Frames 0402- 0406.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the undersigned Attorney, and the Assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

U.S. Patent 6,180,061, to which this application claims priority, and U.S. Patent 6,183,693, containing similar subject matter to the present application, were involved in an infringement action, Cytologix Corporation v Ventana Medical Systems, Inc., for which a decision has been issued by the United States Court of Appeals for the Federal Circuit. U.S. patents 6,541,261 and 6,783,733, both of which contain similar subject matters, were also involved in a separate infringement action, CytoLogix Corp. v. Ventana Medical Systems, Inc., for which a claim construction decision was handed down by the U.S. District Court for the District of Massachusetts on June 20, 2006. Both actions have settled.

III. STATUS OF CLAIMS

Claims 1, 3, 5-8, 10 and 12-18 have been finally rejected. Claims 2, 4, 9 and 11 were canceled. Claims 1, 3, 5-8, 10 and 12-18 are on appeal. A copy of the appealed claims appears in the Claims Appendix of this Brief.

IV. STATUS OF AMENDMENTS

No amendments have been filed subsequent to the rejections in the Office Action mailed January 17, 2008.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention was developed to enable random access processing of multiple microscope slides by applying the reagent to selected slides and controlling heating of the slides according to a protocol under microprocessor control. (Specification at page 11, line 28 through page 12, line 9.)

The claimed invention is exemplified by independent claims 1 and 8. For convenience, both claims are reproduced here.

1. A dispensing assembly, comprising:
   a. a platform supporting a plurality of microscope slides, the platform having plural heated surface areas, each heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide bearing a biological sample;
   b. plural temperature sensors on the platform for sensing temperature of respective heated surface areas;
   c. a liquid dispenser that dispenses liquid reagents onto the slide bearing the biological sample, said liquid dispenser being located above said platform, said liquid dispenser and platform being adapted for relative movement between said liquid dispenser and platform; and
   d. a microprocessor adapted to be programmed with information on the location of the liquid reagents, the location of the slides, and a protocol to control heating of the slides and application of reagents to the slides.

8. A method for processing biological samples mounted on microscope slides, comprising:
   a. programming a microprocessor with information on location of liquid reagents, location of slides and a protocol for applying reagents to slides and heating slides;
   b. placing a microscope slide having a biological sample on a surface area of a platform, the surface area being heated by an electric heater thereunder and the platform being adapted to support a plurality of slides, the platform further comprising plural temperature sensors for sensing temperature of respective surface areas;
   c. under microprocessor control, causing relative movement between a liquid dispenser and the platform so as to align the liquid dispenser over a microscope slide;
   d. under microprocessor control, dispensing liquid reagent from the liquid dispenser onto the slide; and
   e. under microprocessor control, causing heating of the biological samples.

A particular embodiment of Applicants' invention is directed to a dispensing assembly with random access slide staining capability. The dispensing assembly includes a platform and a liquid dispenser. The platform can support a plurality of microscope slides and has plural heated

surface areas, each heated by an electric heater that underlies each heated surface area. This configuration provides for conductive heating of at least one microscope slide bearing a biological sample that is in contact with one of the heated surface areas. The platform further includes plural temperature sensors on the platform for sensing the temperatures of respective heated surface areas.

The liquid dispenser and the platform of this embodiment are adapted for relative movement between the liquid dispenser and the platform. Relative movement between the liquid dispenser and platform could result from either the liquid dispenser or the platform, or both, moving relative to the instrument base.

This embodiment also includes a microprocessor adapted to be programmed with information on the location of the liquid reagents, the location of the slides, and a protocol to control heating of the slides and application of reagents to the slides.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 1, 3, 5-8, 10 and 12-18 are properly rejected under 35 U.S.C. § 103(a) as being obvious over Heidt (US 5,089,229), Copeland (US 5,654,200), Kerr (US 5,075,079) or Rogers (US 4,043,292), each in view of Potter (US 5,819,842).

VII. ARGUMENT

CLAIMS 1, 3, 5-8, 10 AND 12-18 ARE NOT PROPERLY REJECTED UNDER 35 U.S.C. § 103(a) AS BEING OBVIOUS OVER HEIDT, COPELAND, KERR OR ROGERS, EACH IN VIEW OF POTTER

According to the rejection of record, the primary references (Heidt, Copeland, Kerr and Rogers) "are directed to the automated processing of slides encompassing all of the claimed elements except for an individual sensor beneath each slide to control each slides [sic] temperature independently." (November 2, 2006 Office Action at 3.) As discussed more fully below, none of the primary references cited by the Examiner disclose plural heated surface areas, each heated by an electric heater thereunder, wherein each heated surface area is adapted to be in contact with and underlie a microscope slide bearing a biological sample.

Potter is said to teach "an apparatus for manipulation of biological samples on slides" and "an individual sensor below each slide that regulates the temperature of each individual slide."

(Id.) In fact, Potter does not disclose such an apparatus because Potter is not directed to the analysis of biological samples on slides. Instead, as discussed below, Potter is directed to liquid samples contained in wells.

The Examiner has rejected Applicants' argument that one of skill in the art of slide staining had no apparent reason, at the time of the invention, to combine the heating system of Potter with the apparatus disclosed in Heidt, Copeland, Kerr or Rogers. In a previous Office Action, the Examiner stated that "Applicants' also argue the rejection of record is directed to a different method of intended use" and that "[t]hese remarks are not convincing because the method of intended use of an apparatus is of no patentable moment." (Id.) A more accurate description of Applicants' position is that each reference cited by the Examiner must be considered in the context of the state of the art at the time of the invention. Applicants have presented evidence that the heating system of Potter was advantageous for the uses contemplated by Potter (i.e., DNA or RNA amplification, enzyme reactions, and investigating rates of hybridization and melting of nucleic acids), but that there was no apparent reason for one of skill in the art to apply the heating system as described in Potter to the apparatuses disclosed in the primary references.

1. Standard for Determining Obviousness

In *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. ___, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007), the Supreme Court reaffirmed the standard for determining obviousness as set forth in *Graham v. John Deere*, 383 U.S. 1 (1966). In *Graham* the Supreme Court articulated four factual inquiries for determining obviousness.

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.

Graham, 383 U.S. at 17-18.

Additionally, in *KSR*, the Supreme Court, citing *Graham*, warned against the use of hindsight bias in determining obviousness, stating that "[a] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." *Id.* at 17.

In the Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103(a) at MPEP 2141, the U.S.P.T.O. provides that:

> When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions."

2. <u>The Scope and Contents of the Prior Art and the Level of Ordinary Skill in the Art</u>

As stated in the attached Declaration of Ron Zeheb, Ph.D., Under 37 C.F.R. § 1.132, originally submitted with the Amendment filed on October 31, 2007, at the time of the invention, all slide staining processes could be categorized as follows:

A. <u>Routine Staining</u>

Routine staining is performed as a batch process where all slides are treated the same. The slides are typically mounted in baskets that are dipped into buckets of solution. As such, they do not require random access dispensing systems as claimed. Further, they generally do not require heating.

B. <u>Advanced Staining</u>

There are three general categories of advanced staining, commonly known as special stains, immunohistochemistry, and *in situ* hybridization. At the time of the invention, one of ordinary skill would not have predicted the utility of plural heated surface areas, each heated by an electric heater thereunder and having a respective temperature sensor, in a random access dispensing assembly or in a method for processing biological samples mounted on microscope slides.

i. Special Stains

At the time of the invention, special stain techniques often required judgments on the part of the technician, such as color analysis. Namely, the technician dipped the slide in a chemical or dye until the tissue elements acquired a certain specified color, as determined visually. Examples of special stain processes are presented in provided references Luna (1968), Prophet et al. (1992) and Bancroft and Stevens (1996), each of which is an exhibit to the attached Declaration of Ron Zeheb, Ph.D., Under 37 C.F.R. § 1.132. In these exhibits, arrows with asterisks indicate steps in the procedures which must be performed visually and thus require user input. Because such techniques rely highly on the skills of the technician, and are considered an art, they had not been considered appropriate for automatic processing.

ii. Immunohistochemistry

The second type of advanced stain is immunohistochemistry. Apparatuses such as those disclosed in cited references Copeland and Rogers would have been seen by one of skill in the art as being particularly suited to immunohistochemical staining (also called immunostaining). (See e.g., Copeland, column 2, lines 30-39.) As practiced in 1994, immunohistochemical slides were either processed at room temperature (without the application of heat) or were heated to approximately body temperature. In either situation, all of the slides were processed at the same temperature, regardless of the particular histochemical stain. The automated slide stainers on the market by 1994 did one or the other. Examples of automated slide stainers without any heating capability were Fisher's Code-on and Shandon's Cadenza; whereas, Ventana's 320/ES immunohistochemical slide stainer (similar to the Copeland primary reference) heated all of the slides to approximately body temperature.

iii. *in situ* Hybridization

The third category of advanced staining is *in situ* hybridization (ISH). This type of stain requires temperatures that are much higher than body temperature, often in the 70-95°C range. However, the small volume of reagent probe typically used (approximately ten microliters) can rapidly evaporate at such temperatures. To prevent evaporation during ISH processing, the tissue section and the small amount of reagent/probe are sealed on the slide using a coverslip. The edges of the coverslip are sealed with, for example, rubber cement or nail polish. A system in which the sample must be sealed off from the outside environment is mechanically

incompatible with a device that controls relative movement between a liquid dispenser and a platform, and that dispenses liquid reagents onto a microscope slide bearing a biological sample, such as in the claimed dispensing assembly. One of ordinary skill at the time of the invention (1994) would not have considered a system with high temperature heating and a stringent requirement for preventing evaporation of an extremely low volume of reagent as compatible with an open dispensing system.

In the Office Action made Final dated January 17, 2008, the Examiner stated that the Declaration of Dr. Zeheb was "not backed by factual evidence and is not convincing." Id. at 5.

Dr. Zeheb is an expert in the field of histological procedures and is the Director of Diagnostic Molecular Pathology at The Lahey Clinic in Burlington, Massachusetts. Contrary to the Examiner's statements, Dr. Zeheb provides factual evidence supporting his summary of the state of the art at the time of filing. As evidenced by the exhibits attached to Dr. Zeheb's Declaration, Dr. Zeheb considered all staining techniques of which he is aware that were known as of the date of filing. According to Dr. Zeheb, one of ordinary skill in the art would not have considered the present invention as useful for the staining techniques known at the time of filing; nor would one of skill in the art have considered the teachings of any of the references cited by the Examiner alone, or in combination, as likely to succeed in the automated processing of these techniques, in particular, special staining techniques.

3. Teachings of the Cited References

A. Copeland

Copeland teaches an automated immunostaining apparatus having a reagent application zone and a reagent supply zone. The apparatus has a carousel supporting a plurality of slide supports and a drive device that allows for consecutively positioning each of a plurality of slide supports in the reagent application zone (see Abstract). Copeland further describes an embodiment in which the apparatus has a "heating chamber means surrounding the slide support carousel for heating slides supported thereon to a predetermined temperature." (See column 3, lines 8-10.) Thus, Copeland teaches convective heating rather than contact (conductive) heating to heat the slides (column 3, lines 8-22). The slides of Copeland are simply warmed to a common temperature by air that has been heated.

B. Rogers

Rogers teaches an apparatus in which slides are supported on a rotary carousel. Heat is provided using the typical approach of moving the slides into a heated chamber. Specifically, in Figure 4 of Rogers, the heating element 80 provides heat to air blown into the interior of the unit to heat the slides. Figure 6 discloses a radiant heater 90. The support elements 26 on the carousel (Figures 2 and 3 of Rogers) cannot be considered plural heated surface areas, each heated by an electric heater thereunder, because they do not provide heat to the slides. Rather, they simply support the slides within the heated environment.

C. Heidt and Kerr

In both Heidt and Kerr, instead of a reagent dropping onto a microscope slide bearing a biological sample, a drop of serum is dispensed onto various chemical analyte "slides," each of which is impregnated with a reagent that causes a color to develop upon reacting with substances in the serum. The analyte slides are heated to a common temperature by convective heating and are optically analyzed within the system.

The analyte slides in Heidt are described as follows

> When the 10 microliters [of serum] are forced out of the pipette tip, a drop will form and be suspended below the open end 310 of the tip. The pipette lifter assembly is then activated, which will cause the pipette tip 176 to be lowered until the drop touches the film portion 124 of the test slide, where upon, by capillary action, the sample serum will flow onto the analyte film portion of the test slide

(Column 23, lines 57-64).

The analyte slides in Kerr are described as follows:

> Each slide 28 includes a circular analysis or examination area 29 (FIGS. 7, 9 and 10) with an absorbent receiving surface 31 at a top portion 33 of the slide 28 for spotting with a fluid or serum sample. A translucent barrier strip 35 for preventing evaporation and blocking fluid drainage is provided across the analysis area 29 at a bottom surface 37 of the slide 28. Both the receiving surface 31 and the barrier strip 35 are respectively recessed from the top and bottom surfaces 33 and 37 of the slide 28

(Column 5, line 67 through Column 6, line 5).

Based on these teachings, one of skill in the art would not have seen the apparatuses disclosed in Heidt and Kerr as pertaining to the field of microscope slide staining. Furthermore, even if one of skill in the art of slide staining would have considered either Heidt or Kerr, neither reference is any more relevant than Copeland or Rogers.

D. Potter

The device disclosed in Potter was designed for the special needs associated with enzyme reactions, hybridization and melting of nucleic acids, and thermal cycling of samples for amplification of DNA. These types of laboratory techniques require small amounts of expensive or difficult to obtain samples. As such, one of the primary concerns is reduction of evaporation while the samples are being heated and cooled. To prevent condensation and evaporation of the sample, the top of the container is covered with a lid that has heating elements (See column 7, lines 6-12.)

Potter discloses an apparatus capable of independently regulating the heating of each sample in a sample container designed for rapid heat transfer to a set temperature. According to FIGS. 1 and 2 of Potter, within the sample plate 10, the sample 11 is in the form of a thin disc of fluid contained in a well 13. Each well 13 is sealed at the top by sealing foil 15 and sticky seal 17 or heat sealed after the samples 11 are placed in them. The base of the well 13 is likewise shielded.

4. Differences Between the Prior Art and Applicants' Claimed Invention

The Examiner is correct that both Copeland and Rogers relate to microscope slide staining and disclose a liquid dispenser and a means for automating the dispensing of reagents onto a microscope slide. However, as described more fully below, this statement is incorrect with regard to both Heidt and Kerr. Additionally, the Examiner has oversimplified Applicants' invention by stating that the four primary references "are directed to the automated processing of slides encompassing all of the claimed elements except for an individual sensor beneath each slide to control each slides [sic] temperature independently." Office Action made Final, November 2, 2006 at 3.

None of the primary references, Heidt, Copeland, Kerr or Rogers, discloses a platform supporting a plurality of microscope slides, the platform having plural heated surface areas, each heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide bearing a biological sample and having plural temperature

sensors on the platform for sensing temperature of respective heated surface areas as claimed in the present application.

As described above, for most embodiments, the primary references rely on convective heating to heat the slides rather than conductive heating enabled by the claimed plural underlying heated surface areas.

In rejecting Applicant's argument that the cited prior art does not teach conductive slide heating, the Examiner stated that "the pending claims are only directed to 'heating' and do not specify conductive heating." Office Action made Final, January 17, 2008 at 3. Although the claims do not explicitly recite the term "conductive heating," conductive heating is specified by the claimed structure. Specifically, all of the independent claims clearly specify surface areas being heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide. Thus, the microscope slides are heated in a manner that is not taught in the prior art.

Rogers does illustrate, in one embodiment represented by Figures 7 and 8, the conductive approach to heating. However, in the embodiment disclosed in Figures 7 and 8, slides are slowly advanced across a stationary platen 94. There is no suggestion of plural heated surface areas, each heated by an electric heater and underlying a microscope slide with temperature sensed by a respective temperature sensor. Furthermore, in this embodiment, Rogers teaches that "[t]he various reactants are applied to the specimen-containing surfaces of the slides through orifices in the platen." Rogers does not teach a liquid dispenser that dispenses liquid reagent onto the slide that bears the biological sample, said liquid dispenser being located above the platform.

Additionally, as discussed below, neither Heidt nor Kerr relates to microscope slide staining. Instead, each is directed to an apparatus used in the analysis of blood in which a drop of serum is dispensed onto a chemically reactive analyte slide.

Potter also does not relate to microscope slide staining and fails to teach a dispensing assembly that includes a platform and a liquid dispenser, wherein the platform can support a plurality of microscope slides. In fact, Potter does not disclose a liquid dispenser. As such, Potter fails to disclose a dispensing assembly with random access slide staining capability.

5. Without Improper Hindsight Bias, There was no Apparent Reason to Combine the Heating System of Potter with the Apparatus of Heidt, Copeland, Kerr or Rogers

In *KSR*, the Supreme Court relied upon two references, both directed to the same field of endeavor as the claimed invention (accelerator pedals) for its determination of obviousness. The fact that both references were directed to the same field of endeavor as the invention made it much more likely that one of skill in the art would have found an apparent reason to combine the references to gain the advantages of both references.

In this case, on the other hand, the Examiner has cited five different references to support his rejection under 35 U.S.C. §103(a). Of those references, only two, Copeland and Rogers, actually relate to the same field of endeavor as Applicants' claimed invention (microscope slide staining). Heidt and Kerr, discussed *supra*, relate to the field of chemical analysis of blood, while Potter, also discussed *supra*, relates to the fields of enzyme reactions, hybridization and melting of nucleic acids, and thermal cycling of samples for amplification of DNA. Because Potter does not relate to the same field of endeavor, there is less likelihood that one of skill in the art would have found any apparent reason for combining its heating system with any of Heidt, Copeland, Kerr or Rogers.

In fact, Applicants have provided ample evidence that, at the time of the invention, there was no perceived need for a microscope slide stainer having random access dispensing assembly comprising plural heated surface areas, each heated by an electric heater thereunder and having plural temperature sensors for sensing temperature of respective surface areas. Without an apparent reason for combining Potter with any of the primary references, the Examiner has based the 103(a) rejection upon improper hindsight bias to identify portions of the invention from a different field of endeavor.

Histochemical staining of biological samples as in Copeland and Rogers requires sequential application of at least one stain and a wash solution to remove the excess stain. Actually, almost all histochemical processes require multiple stains or reagents, interspersed by washes. A system in which the samples are sealed off from the outside environment in sample wells, like the apparatus described in Potter, would not be compatible with the needs associated with automated microscope slide staining protocols. Thus, one of skill in the art would not look to Potter when designing a dispensing assembly wherein liquid reagents are dispensed onto the microscope slides from above as claimed in the present invention.

Furthermore, Potter describes a heating block adapted for specially designed microplate wells containing liquid samples. Potter does not describe staining of tissue sections on microscope slides. Potter makes no mention of slides, histochemistry, or tissue samples. Instead, Potter relates to analyzing a liquid sample 11 (Column 3, lines 55-56). The samples are in wells 13, such as in a microplate format (Column 3, lines 61-63; Column 7, lines 5, 11, and 18-21; Fig. 1). Unlike a transparent, rigid, low thermal conductivity microscope slide, Potter teaches that the sample is placed on foil 12 for its high thermal conductivity (Column 3, lines 56-58). Further, metal foils are neither transparent nor rigid. These differences emphasize the fact that Potter discloses an apparatus for uses that are quite different from histochemical staining of tissue samples. The reasons stated in the specification of Potter (Column 1, line 9 through Column 2, line 29) regarding the desirability for varying the temperature of samples must be viewed in the context of liquid biological samples, and do not translate to slide staining. The teachings of Potter do not provide a reason for one of ordinary skill in the art of slide staining to combine Potter with the cited primary art references.

On the other hand, within the field of slide staining described above in Section B, there was no apparent reason for conductive heating using a platform supporting a plurality of microscope slides, the platform having plural heated surface areas, each heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide bearing a biological sample and the platform having plural temperature sensors for sensing temperature of respective heated surface areas.

In fact, the device disclosed in Potter would be unsuitable for use with slide staining, and the apparatuses described in Heidt, Copeland, Kerr and Rogers are incompatible with the laboratory techniques involving liquid samples as envisioned by Potter.

Additionally, the heating control of Potter would be contrary to the reaction conditions required by the chemical analyte slides described in Heidt and Kerr. Both Heidt and Kerr disclose devices for use in clinical chemistry for measuring the concentrations of various chemicals in blood. Analysis of the chemical analyte slides does not require the heating control as disclosed in Potter. In fact, in order to accurately analyze such slides, the temperature at which each slide is incubated must be the same.

For these reasons, the heating control taught by Potter is not meaningful in the context of slide staining or in the context of analysis of chemical analyte slides. At the time of the

invention, the benefits of plural heating surfaces in a PCR cycler as proposed by Potter were not recognized as having any meaningful benefits in the field of slide staining.

Additionally, the inclusion of plural heated surface areas, each heated by an electric heater thereunder in a random access dispensing system imposes significantly greater technical challenges and expense. As such, one of ordinary skill in the art would need a compelling reason to undertake the technological and economic challenges associated with such modifications. As described above, in 1994 (the year of filing), no such compelling need existed.

6. <u>A combination of any of the primary references with Potter would not result in the claimed invention</u>

Even if one of skill in the art had found motivation to combine Potter with any of the primary references, the result would not have been the claimed invention.

In particular, none of the references, alone or in combination teach a platform supporting a plurality of microscope slides, the platform having plural heated surface areas, each heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide bearing a biological sample.

Furthermore, even if one of skill in the art had found a reason to combine the heating system of Potter with either Heidt or Kerr, the invention as claimed would not result because none of the references are directed to microscope slides bearing a biological sample.

Instead, as described above, Heidt and Kerr are both directed to the analysis of chemical analyte slides upon which a drop of serum is dispensed. The chemical analyte slide of Heidt and Kerr comprises reagent used for chemical analysis of blood.

Potter is directed to analysis of liquid samples in wells.

The Examiner argues in the Office Action made Final dated January 17, 2008 that the claims are broad enough to encompass "any structure that supports a biological sample, such as [a] well." Each of the pending claims recites not just a slide, but a microscope slide. One of ordinary skill in the art would not equate a slide, specifically a microscope slide, with a well. A microscope slide is a flat surface upon which a sample is placed, as depicted in Figures 19A and 19B. Additionally, the common definition of microscope slide is "a <u>flat</u> piece of glass on which an object is mounted for microscopic examination." (Webster's Ninth New Collegiate Dictionary, Merriam-Webster Inc., Springfield, MA 1986)(emphasis added) (attached hereto). Thus, none of Heidt, Kerr or Potter are directed to microscope slides bearing a biological sample.

There is no evidence to suggest that one of skill in the art would have found it obvious to modify any of Heidt, Kerr or Potter to accommodate a microscope slide bearing a biological sample.

Additionally, in order to accurately analyze the chemical analyte slides of Heidt or Kerr, the temperature at which each slide is incubated must be identical. Therefore, the heating control of Potter would be contrary to the reaction conditions required for analysis of chemical analyte slides. In view of this fact, Heidt and Kerr teach away from any combination with Potter.

7. <u>Contrary to the Expectations of Those of Skill in the Art, Applicants' Invention Enabled Automation of Special Stains</u>

One of the main advantages of the present invention is that it enabled automation of special stains. Prior to automation, special stain techniques often required judgments on the part of the technician, such as color analysis. Namely, the technician dipped the slide in a chemical or dye until the tissue elements acquired a certain specified color, as determined visually. Because such techniques rely heavily on the skills of the technician, and are considered an art, they had not been considered appropriate for automatic processing.

As the system was further described with independent temperature control (later application number 09/032,676, now U.S. Patent No.: 6,183,693), Applicants recognized that even special stain processes could be performed in an automated system by strictly controlling variables such as reagent concentration (disposing of the reagent after use instead of re-using it, which was previously the most common practice), temperature and incubation time. Contrary to beliefs of those skilled in the art, precise control could take the place of the art required prior to the present invention and such precise control was enabled by the claimed invention.

CONCLUSION

Claims 1, 3, 5-8, 10 and 12-18 comply with the requirements of 35 U.S.C. § 103(a) and are not obvious over Heidt, Copeland, Kerr or Rogers in view of Potter. In view of the foregoing arguments and legal authority, reversal of the rejection is requested.

Respectfully submitted,

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VIII. CLAIMS APPENDIX

1. A dispensing assembly, comprising:

   a. a platform supporting a plurality of microscope slides, the platform having plural heated surface areas, each heated by an electric heater thereunder, each heated surface area being adapted to be in contact with and underlie a microscope slide bearing a biological sample;

   b. plural temperature sensors on the platform for sensing temperature of respective heated surface areas;

   c. a liquid dispenser that dispenses liquid reagents onto the slide bearing the biological sample, said liquid dispenser being located above said platform, said liquid dispenser and platform being adapted for relative movement between said liquid dispenser and platform; and

   d. a microprocessor adapted to be programmed with information on the location of the liquid reagents, the location of the slides, and a protocol to control heating of the slides and application of reagents to the slides.

3. A dispensing assembly as claimed in claim 1, wherein the heated surface area is adapted to support only one slide.

5. A dispensing assembly as claimed in claim 1, wherein the platform comprises plural removable slide supports.

6. A dispensing assembly as claimed in claim 1, wherein the heater is a resistive heating element.

7. A dispensing assembly as claimed in claim 1, wherein the liquid dispenser further includes an actuator positioned at a stationary liquid dispensing station, the platform being moved to index slides to the liquid dispensing station.

8. A method for processing biological samples mounted on microscope slides, comprising:

a. programming a microprocessor with information on location of liquid reagents, location of slides and a protocol for applying reagents to slides and heating slides;

b. placing a microscope slide having a biological sample on a surface area of a platform, the surface area being heated by an electric heater thereunder and the platform being adapted to support a plurality of slides, the platform further comprising plural temperature sensors for sensing temperature of respective surface areas;

c. under microprocessor control, causing relative movement between a liquid dispenser and the platform so as to align the liquid dispenser over a microscope slide;

d. under microprocessor control, dispensing liquid reagent from the liquid dispenser onto the slide; and

e. under microprocessor control, causing heating of the biological samples.

10. A method as claimed in claim 8 wherein each heated surface area supports only one slide.

12. A method as claimed in claim 8 wherein plural removable slide supports are on the platform.

13. A method as claimed in claim 8 wherein the heater is a resistive heating element.

14. A method as claimed in claim 8 wherein the liquid dispenser includes an actuator positioned at a stationary liquid dispensing station, the platform being moved to index slides to the liquid dispensing station.

15. A dispensing assembly as claimed in claim 1, wherein the platform is a moveable platform.

16. A dispensing assembly as claimed in claim 15, wherein the moveable platform is a carousel.

17. A method as claimed in claim 8, wherein the platform is a moveable platform.

18. A method as claimed in claim 17, wherein the moveable platform is a carousel.

IX. EVIDENCE APPENDIX

1. Declaration of Ron Zeheb, Ph.D., Under 37 C.F.R. § 1.132, including Exhibits A-C.

   A copy of this Declaration was provided with Request for Continued Examination and Amendment filed on October 31, 2007.

2. Webster's Ninth New Collegiate Dictionary, Merriam-Webster Inc., Springfield, MA 1986. (definition of "slide").

X. RELATED PROCEEDINGS APPENDIX

1. United States Court of Appeals for the Federal Court, *Cytologix Corporation v. Ventana Medical Systems, Inc.*, Case No. 04-1446, Decision decided September 21, 2005, pp: 1-18.

   This decision was provided as Reference AW with the Supplemental Information Disclosure Statement entered into the record on February 14, 2006.

2. United States District Court for the District of Massachusetts, CytoLogix Corporation v Ventana Medical Systems, Inc., No. 04-11783-RWZ, Memorandum of the Decision issued June 20, 2006, pp. 1-7.

   A copy of this decision was provided with the Amendment filed in the present application on August 17, 2006.